(54) Title: AZA–BICYCLES WHICH MODULATE THE INHIBITION OF CELL ADHESION

(I)

(57) Abstract

The invention is directed to physiologically active compounds of formula (I) wherein R^1 represents R^3-Z^3-, $R^3-L^2-R^4-Z^3-$, $R^3-L^3-Ar^1-L^4-Z^3-$ or $R^3-L^3-Ar^1-L^2-R^4-Z^3-$; R^2 represents hydrogen, halogen, lower alkyl or lower alkoxy; A^1 represents a straight chain C_{1-3}alkylene linkage optionally substituted by one or more groups chosen from alkyl, aryl, arylalkyl, heteroaryl, heteroarylalkyl, imino, oxo, thioxo, or alkyl substituted by $-ZR^6$, $-NY^1Y^2$, $-CO_2R^6$ or $-C(=O)-NY^1Y^2$; L^1 represents a direct bond; an alkenylene, alkylene, alkynylene, cycloalkenylene, cycloalkylene, heteroaryldiyl, heterocycloalkylene or arylene linkage each optionally substituted by (a) an acidic functional group, cyano, oxo, $-S(O)_mR^9$, R^3, $-C(=O)-R^3$, $-C(=O)-OR^3$, $-N(R^8)-C(=O)-R^9$, $-N(R^8)-C(=O)-OR^3$, $-N(R^8)-SO_2-R^9$, $-NY^4Y^5$ or $-[C(=O)-N(R^{10})-C(R^5)(R^{11})]_p-C(=O)-NY^4Y^5$, or by (b) alkyl substituted by an acidic functional group, or by $S(O)_mR^9$, $-C(=O)-NY^4Y^5$ or $-NY^4Y^5$; a $-Z^2-R^{12}-$ linkage; a $-C(=O)-CH_2-C(=O)-$ linkage; a $-R^{12}-Z^2-R^{12}-$ linkage; a $-C(R^4)(R^{13})-[C(=O)-N(R^{10})-C(R^5)(R^{11})]_p-$ linkage; or a $-L^5-L^6-L^7-$ linkage; Z^1 is $C(R^7)(R^{7a})$, $C(=O)$ or $CH(OH)$; Y is carboxy or an acid bioisostere; and the corresponding N–oxides, and their prodrugs; and pharmaceutically acceptable salts and solvates of such compounds and their N–oxides and prodrugs. Such compounds have valuable pharmaceutical properties, in particular the ability to regulate the interaction of VCAM–1 and fibronectin with the integrin VLA–4 ($\alpha 4\beta 1$).